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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/607,108	06/25/2003	Wei-Min Liu	3503.1	3630

22886 7590 08/05/2005

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EXAMINER	
SMITH, CAROLYN L	
ART UNIT	**PAPER NUMBER**
1631	

DATE MAILED: 08/05/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/607,108	LIU ET AL.	
	Examiner	Art Unit	
	Carolyn L. Smith	1631	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-16* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-16* is/are rejected.

7)☒ Claim(s) *1,8, 9, and 15* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *25 June 2003* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Claims 1-16 are under examination.

Specification

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The present title is directed to methods and computer software products for analyzing genotyping data, whereas in contrast the instant claims are specifically directed to methods for analyzing genotyping data.

Claim Objections

Claims 1, 8, 9, and 15 are objected to because of the following minor informalities: The term "medioids" is misspelled on line 6 of claim 1. Claims 1 (lines 4 and 8) and 9 (line 3) are objected to due to the citing of an abbreviation, such as SNP. Correction is suggested by amending in the full name in parentheses. Claims 8 and 15 recite the phrase "a sample covariance matrices" which does not make sense as the "a" is in the singular form while "matrices" is in the plural form. Appropriate correction is requested.

Double Patenting

The nonstatutory double patenting rejection is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent and to prevent possible harassment by multiple assignees. See *In re Goodman*, 11 F.3d 1046, 29 USPQ2d 2010 (Fed. Cir. 1993); *In re Longi*, 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); *In re Van Ornum*, 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Vogel*, 422 F.2d 438, 164 USPQ 619 (CCPA 1970);and, *In re Thorington*, 418 F.2d 528, 163 USPQ 644 (CCPA 1969).

A timely filed terminal disclaimer in compliance with 37 CFR 1.321(c) may be used to overcome an actual or provisional rejection based on a nonstatutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CFR 1.130(b).

Effective January 1, 1994, a registered attorney or agent of record may sign a terminal disclaimer. A terminal disclaimer signed by the assignee must fully comply with 37 CFR 3.73(b).

Claims 1-16 are provisionally rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-16 of copending Application No. 10/850183 in view of Schork et al. (US 2002/0077775 A1).

Claims 1-16 discloses a computer software product comprising a computer readable medium having computer-executable instructions for performing the logical steps of two methods for analyzing genotyping data. The method steps in the instant application are exactly the same as the logic steps claimed in application 10/850183. The only difference between the claims in these applications is the fact that application 10/850183 is directed to a computer software product to implement the methods.

Schork et al. describe methods involving statistically analysis of single nucleotide polymorphisms (SNPs) via the use of software programs including computer software products comprising a computer readable medium having computer-executable instructions (paragraphs 0016 and 0028).

Schork et al. state as methods for polymorphism discovery and mass genotyping continue to provide enormous amounts of information, the challenge shifts to developing methods that best utilize this information, including statistical tests, to provide important information regarding etiology and pathogenesis of common diseases which can elucidate new pathways and molecules to yield new approaches to treatment and prevention therapies (paragraph 0007).

Schork et al. state currently available software programs are computationally inefficient and impractical for doing large association studies (paragraph 0015). It would have been obvious to the person of ordinary skill in the art at the time the invention was made to place software instructions on a programmed storage device (as stated by Schork et al.) for methods involving statistical tests (as stated in the claims of the instant invention) in order to assess statistical significance (as stated by Schork et al., paragraph 0028). A person of ordinary skill in the art would have been motivated to execute the program on the computer readable medium of the copending application resulting in the claimed method, because it would provide efficient ways for doing several thousands of analyses necessary for association studies involving statistical analysis drawn among groups (Schork et al., paragraph 0016). Schork et al. document that one of ordinary skill in the art routinely executes programs to perform statistical analysis on SNPs.

This is a provisional obviousness-type double patenting rejection.

Claim Rejections - 35 USC § 101

35 U.S.C. 101 reads as follows:

> Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.

Claims 1-16 are rejected under 35 U.S.C. 101 because the claimed invention is directed to non-statutory subject matter.

Claims 1-16 are directed to computerized methods for analyzing genotyping data comprising a series of mathematical steps for data manipulation, equivalent to mental processes.

Applicants are reminded that mental processes are not statutory subject matter under 35 USC 101.

The claimed computer-implemented methods are not statutory as any computer implemented method must produce a result which is concrete, tangible, and useful. As set forth in MPEP 2106.IV.B:

"In practical terms, claims define nonstatutory processes if they:

– consist solely of mathematical operations without some claimed practical application (i.e., executing a "mathematical algorithm"); or

– simply manipulate abstract ideas, e.g., a bid (Schrader, 22 F.3d at 293-94, 30 USPQ2d at 1458-59) or a bubble hierarchy (Warmerdam, 33 F.3d at 1360, 31 USPQ2d at 1759), without some claimed practical application."

As set forth in MPEP 2106.IV.B.2(b) (ii):

"A claim is limited to a practical application when the method, as claimed, produces a concrete, tangible and useful result; i.e., the method recites a step or act of producing something that is concrete, tangible and useful. See AT &T, 172 F.3d at 1358, 50 USPQ2d at 1452.

The MPEP § 2106 (IV)(B)(2)(b)(ii) states the following example:

A computer process that simply calculates a mathematical algorithm that models noise is nonstatutory. However, a claimed process for digitally filtering noise employing the mathematical algorithm is statutory.

Comparing the above scenario to claims 1-16, the claimed methods that merely performs imputes probe intensities, performing feature extraction and mathematical analysis, and building

a model is comparable to the nonstatutory example given above as it does not appear to have a valid practical application applied to the imputing, performing, and model building (which can be interpreted to take place solely on the computer). The claimed invention falls more into the example of noise analysis. In this example, it is not until the noise is filtered that a practical application is clearly expressed. It is noted that "practical application" is interpreted to be either a physical phenomena taking place or the representation of a physical phenomena or step.

Claims Rejected Under 35 U.S.C. § 112, Second Paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-16 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which the applicant regards as the invention.

Claims 1 (line 3) and 9 (line 2) recite the phrases "imputing probe intensities" and "imputing in probe intensities", respectively, which are vague and indefinite. According to the online Merriam-Webster dictionary, "impute" is defined as "to inlay the responsibility or blame" as well as "to credit to a person or cause". It is unclear what "imputing probe intensities" and "imputing in probe intensities" is intended to mean. Clarification of this issue via clearer claim wording is requested. Claims 2-8 and 10-16 are also rejected due to their direct or indirect dependency from claims 1 and 9.

Claim 1 is indefinite because it lacks a positive step that correlates the preamble with the active steps of the claimed method. For example, the preamble of the claim recites "A computerized method for building a model for analyzing genotyping data"; however, the final step recites "Building a SNP model". It is unclear as to how building a SNP model results in analyzing genotyping data. A similar issue is also found in instant claim 9. Clarification of this issue via clearer claim wording is requested. Claims 2-8 and 10-16 are also rejected due to their direct or indirect dependency from claims 1 and 9.

Claim 2 recites the phrase "calculating average silhouette width" which is vague and indefinite. It is unclear to what the width belongs. Clarification of the metes and bounds of the claim via clearer claim wording is requested.

Claim 16 recites the limitation "the classification quality" in lines 1-2. There is insufficient antecedent basis for this limitation in the claim as there is no prior mention of a classification quality. It is also unclear what is being assigned this quality. Clarification of these issues via clearer claim wording is requested.

Claim Rejections – 35 USC §102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless –

> (e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

Claims 1-16 are rejected under 35 U.S.C. 102(e)(1) as being anticipated by Kennedy (US 2003/0186280 A1) with support from online Merriam-Webster dictionary definitions ("model" and "relative", 2005).

Kennedy discloses computer program products and software for methods including genotyping SNPs, determining allele frequencies between populations, as well as probe design, data management, analysis, and instrument operation (abstract and paragraph 0038), as stated in instant claims 1 and 9. Kennedy discloses methods to detect genes or genomic regions of biological importance (paragraph 0004). Kennedy discloses constructing arrays of more than 500,000 probe sequences which access large quantities of genetic information by relying on specific hybridization of nucleic acids in samples (paragraph 0078) as well as signal detection of hybridization, processing intensity data (paragraphs 0035-0036), and primers interrogating SNPs (paragraph 0110) which represent imputing probe intensities from multiple samples, wherein the probes are designed to interrogate a SNP, as stated in instant claims 1 and 9. Kennedy discloses determining genome-wide SNP parameters for three populations (African-American, Caucasian, and Asian) followed by close examination of a subset of SNPs showing extreme differences in allele frequency amongst the three populations as well as performing correlations and departure from neutrality estimations (paragraph 0093, Table 1, Figures 5a-d and 6-8) which represents performing a feature extraction on the probe intensities, as stated in instant claims 1 and 9. Merriam-Webster online dictionary defines "model" as an image, structural design, and a system

of data presented as a mathematical description of an entity (see attached definition sheet). Kennedy discloses an image of a hybridized array showing robust signal intensities involving SNPs (paragraph 0083 and Figures 2a-c) as well as classification analysis (paragraph 0084) which represents the building of a SNP model and performing model based classification, as stated in instant claims 1 and 2. Kennedy discloses obtaining genome-wide allele frequency data on a variety of populations that can create a large-scale catalogue of human diversity and uncover departures from neutral models of evolution (paragraph 0111). Kennedy discloses designing arrays to interrogate SNPs (paragraph 0114) which represents model building. Kennedy discloses calculating normalized discrimination (PM-MM)/(PM+MM) which represents a measure of sequence specificity to be used in the detection filter of the genotype calling algorithm (paragraph 0114) which represents a multivariate normal model, as stated in instant claims 7 and 14. The departure from neutrality estimations from array data involving pairwise comparisons (paragraph 0093 and Figure 5b) represent sample covariance matrices, as stated in instant claims 8 and 15. Kennedy discloses arrays (paragraph 0013 and Figure 2) as well as calculating a silhouette width as a relative measure of the difference between the distance of the data point to the nearest neighbor group and the distance of the data point to other data points in the same group (paragraph 0118) and evaluating the quality of classification of with the average silhouette width as well as cluster visualization of SNPs for each sample on both strands plotted in two dimensions (paragraphs 0084 and 0014, Figures 3a-d), as stated in instant claim 2, which also represents sample covariance matrices, as stated in instant claims 8 and 15. Kennedy discloses a range of silhouette widths from –1 to 1 wherein the larger the width results in better classification from a clustering point of view (paragraphs 0118 and 0084) which represents a

quantification of the quality of the classification, as stated in instant claims 2 and 16. Kennedy discloses using an algorithm that includes a signal detection filter based on Wilcoxon's signed rank test (representing a ranked-based analysis), classification using partitioning around medoids (PAM), and the computation of several quality scores, (paragraph 0118) as well as SNP ranking (paragraph 0085), as stated in instant claims 1, 3, 5, 10, and 12. The term "relative" is defined by the Merriam-Webster online dictionary as expressed as the ratio of the specified quantity to the total magnitude (see attached definition sheet). Kennedy discloses the distribution of heterozygosity in three populations separated into 10 bins plus a zero bin versus the percentage of scored SNPs (Figure 5a, paragraph 0016) as well as ranking F_{ST} values for each pairwise comparison (Figure 5b, paragraphs 0017 and 0095) which represents a relative sum of signed ranks, as stated in instant claims 4 and 11. Kennedy discloses calculating RAS as the median of the ratios Ai/(Ai + Bi), where Ai and Bi are signals of A and B alleles of the ith probe quartet (paragraph 0118) which represents estimating a relative allele signal (RAS), as stated in instant claims 6 and 13.

Thus, Kennedy anticipates the limitations in claims 1-16.

Conclusion

No claim is allowed.

Papers related to this application may be submitted to Technical Center 1600 by facsimile transmission. Papers should be faxed to Technical Center 1600 via the PTO Fax Center. The faxing of such papers must conform with the notices published in the Official Gazette, 1096 OG 30 (November 15, 1988), 1156 OG 61 (November 16, 1993), and 1157 OG 94 (December 28,

1993) (See 37 CFR §1.6(d)). The Central Fax Center number for official correspondence is (571) 273-8300.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Carolyn Smith, whose telephone number is (571) 272-0721. The examiner can normally be reached Monday through Thursday from 8 A.M. to 6:30 P.M.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Ardin Marschel, can be reached on (571) 272-0718.

Any inquiry of a general nature or relating to the status of this application should be directed to Legal Instruments Examiner Tina Plunkett whose telephone number is (571) 272-0549.

August 1, 2005

MARJORIE A. MORAN
PRIMARY EXAMINER
Marjorie A. Moran
8/2/05